

CLAIMS

WHAT IS CLAIMED IS:

1. A method of alleviating a symptom of a disorder characterized by reduced levels of hematopoiesis comprising: administering an ephrin inhibitor selected from the group consisting of a soluble ephrin and a small molecule to a patient suffering from reduced levels of hematopoiesis, wherein the administered soluble ephrin or small molecule increases proliferation of hematopoietic cells, thereby alleviating the symptom of the disorder.
2. The method of claim 1, wherein the soluble ephrin is selected from the group consisting of soluble ephrin-A2 and soluble ephrin-B2.
3. The method of claim 1, wherein the soluble ephrin or a fragment thereof is joined to a heterologous amino acid sequence.
4. The method of claim 3, wherein the heterologous amino acid sequence comprises a constant domain of an immunoglobulin.
5. The method of claim 1, wherein the disorder is selected from the group consisting of leukopenia, lymphocytopenia, neutropenia, granulocytopenia, agranulocytosis, thrombocytopenia, coagulation factor deficiencies, hypoproliferative anemias, hypoplastic anemias, cancer-induced anemias, chemotherapy-induced anemias, radiation-induced anemias, sepsis-induced anemias, Fanconi's anemia, and anemia associated with Blackfan-Diamond syndrome.
6. The method of claim 1, wherein the soluble ephrin is administered in an amount selected from the group consisting of at least 0.1 ng/kg/day, at least 1 ng/kg/day, at least 5 mg/kg/day, at least 10 mg/kg/day, and at least 50 mg/kg/day.
7. The method of claim 1, wherein the soluble ephrin is locally administered to bone marrow.

8. The method of claim 1, wherein the soluble ephrin is administered to achieve a tissue concentration of 0.1 nM to 100 nM.
9. The method of claim 1, wherein the soluble ephrin is administered by injection.
10. The method of claim 1, wherein the soluble ephrin is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.
11. The method of claim 1, wherein the soluble ephrin is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.
12. A method of alleviating a symptom of a disorder characterized by reduced levels of hematopoiesis comprising: administering an antibody or affibody that specifically binds to an ephrin or ephrin receptor to a patient suffering from reduced levels of hematopoiesis, wherein the administered antibody or affibody increases proliferation of hematopoietic cells, thereby alleviating a symptom of the disorder.
13. The method of claim 12, wherein the ephrin is selected from the group consisting of ephrin-A2 and ephrin-B2.
14. The method of claim 12, wherein the disorder is selected from the group consisting of leukopenia, lymphocytopenia, neutropenia, granulocytopenia, agranulocytosis, thrombocytopenia, coagulation factor deficiencies, hypoproliferative anemias, hypoplastic anemias, cancer-induced anemias, chemotherapy-induced anemias, radiation-induced anemias, sepsis-induced anemias, Fanconi's anemia, and anemia associated with Blackfan-Diamond syndrome.
15. The method of claim 12, wherein the antibody is selected from the group consisting of polyclonal, monoclonal, chimeric, oligomeric, single chain, F_{ab} , F_{ab}' , and $F_{(ab)2}$ antibodies.

16. The method of claim 12, wherein the antibody or affibody is administered in an amount selected from the group consisting of at least 0.1 ng/kg/day, at least 1 ng/kg/day, at least 5 mg/kg/day, at least 10 mg/kg/day, and at least 50 mg/kg/day.
17. The method of claim 12, wherein the antibody or affibody is locally administered to bone marrow.
18. The method of claim 12, wherein the antibody or affibody is administered to achieve a tissue concentration of 0.1 nM to 100 nM.
19. The method of claim 12, wherein the antibody or affibody is administered by injection.
20. The method of claim 12, wherein the antibody or affibody is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.
21. The method of claim 12, wherein the antibody or affibody is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.
22. A method of alleviating a symptom of a disorder characterized by increased levels of cellular proliferation in an intestinal tract comprising: administering an ephrin inhibitor selected from the group consisting of a soluble ephrin and a small molecule to a patient suffering from increased levels of cellular proliferation in a intestinal tract, wherein the administered soluble ephrin or small molecule reduces proliferation of intestinal cells, thereby alleviating the symptom of the disorder.
23. The method of claim 22, wherein the soluble ephrin is selected from the group consisting of a soluble ephrin-A2 and soluble ephrin-B2.
24. The method of claim 22, wherein the soluble ephrin or a fragment thereof is joined to a heterologous amino acid sequence.

25. The method of claim 24, wherein the heterologous amino acid sequence comprises a constant domain of an immunoglobulin.
26. The method of claim 22, wherein the disorder is selected from the group consisting of growths and polyps of the large intestine, colorectal cancers, anorectal cancers, small intestine tumors, Gardner's syndrome, Peutz-Jeghers syndrome, Rendu-Osler-Weber syndrome, Bowen's disease, Crohn disease, ulcerative colitis, irritable bowel syndrome and extramammary Paget's disease.
27. The method of claim 22, wherein the soluble ephrin is administered in an amount selected from the group consisting of at least 0.1 ng/kg/day, at least 1 ng/kg/day, at least 5 mg/kg/day, at least 10 mg/kg/day, and at least 50 mg/kg/day.
28. The method of claim 22, wherein the soluble ephrin is locally administered to an intestinal tract tissue.
29. The method of claim 22, wherein the soluble ephrin is administered to achieve a tissue concentration of 0.1 nM to 100 nM.
30. The method of claim 22, wherein the soluble ephrin is administered by injection.
31. The method of claim 22, wherein the soluble ephrin is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.
32. The method of claim 22, wherein the soluble ephrin is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.
33. A method of alleviating a symptom of a disorder characterized by increased levels of cellular proliferation in an intestinal tract comprising: administering an antibody or affibody that specifically binds to an ephrin or ephrin receptor to a patient suffering from increased levels of cellular proliferation in an intestinal tract, wherein the

administered antibody or affibody reduces proliferation of intestinal cells, thereby treating the disease or disorder.

34. The method of claim 33, wherein the ephrin is selected from the group consisting of ephrin-A2 and ephrin-B2.
35. The method of claim 33, wherein the disorder is selected from the group consisting of growths and polyps of the large intestine, colorectal cancers, anorectal cancers, small intestine tumors, Gardner's syndrome, Peutz-Jeghers syndrome, Rendu-Osler-Weber syndrome, Bowen's disease, and extramammary Paget's disease.
36. The method of claim 33, wherein the antibody is selected from the group consisting of polyclonal, monoclonal, chimeric, oligomeric, single chain, F_{ab}, F_{ab}', and F_{(ab')₂} antibodies.
37. The method of claim 33, wherein the antibody or affibody is administered in an amount selected from the group consisting of at least 0.1 ng/kg/day, at least 1 ng/kg/day, at least 5 mg/kg/day, at least 10 mg/kg/day, and at least 50 mg/kg/day.
38. The method of claim 33, wherein the antibody or affibody is locally administered to intestinal tract tissue.
39. The method of claim 33, wherein the antibody or affibody is administered to achieve a tissue concentration of 0.1 nM to 100 nM.
40. The method of claim 33, wherein the antibody or affibody is administered by injection.
41. The method of claim 33, wherein the antibody or affibody is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.

42. The method of claim 33, wherein the antibody or affibody is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.
43. A method of alleviating a symptom of a disorder characterized by an abnormal level of cellular proliferation in a tissue: administering an ephrin inhibitor selected from the group consisting of a soluble ephrin and a small molecule to a patient suffering from abnormal levels of cellular proliferation in the tissue, wherein the administered soluble ephrin or small molecule modulates proliferation of cells in the tissue, thereby alleviating the symptom of the disorder.
44. The method of claim 43 wherein the tissue is selected from the group consisting of skin, retina, prostate, and ovarian tissue.
45. The method of claim 43, wherein the soluble ephrin is selected from the group consisting of a soluble ephrin-A2 and soluble ephrin-B2.
46. The method of claim 43, wherein the soluble ephrin or a fragment thereof is joined to a heterologous amino acid sequence.
47. The method of claim 46, wherein the heterologous amino acid sequence comprises a constant domain of an immunoglobulin.
48. The method of claim 43, wherein the disorder is selected from the group consisting of psoriasis, inflammatory skin disease, skin cancer, skin atrophy, benign prostate hypoplasia, prostate cancer, polycystic ovary syndrome, ovarian cancer.
49. The method of claim 43, wherein the soluble ephrin is administered in an amount selected from the group consisting of at least 0.1 ng/kg/day, at least 1 ng/kg/day, at least 5 mg/kg/day, at least 10 mg/kg/day, and at least 50 mg/kg/day.
50. The method of claim 43, wherein the soluble ephrin is locally administered to a tissue selected from the group consisting of skin, prostate, and ovarian tissue.

51. The method of claim 43, wherein the soluble ephrin is administered to achieve a tissue concentration of 0.1 nM to 100 nM.
52. The method of claim 42, wherein the soluble ephrin is administered by injection.
53. The method of claim 43, wherein the soluble ephrin is administered by a route selected from the group consisting of oral, subcutaneous, intraperitoneal, intramuscular, intracerebroventricular, intraparenchymal, intrathecal, intracranial, buccal, mucosal, nasal, and rectal administration.
54. The method of claim 43, wherein the soluble ephrin is formulated into a pharmaceutical composition comprising a physiologically acceptable carrier, excipient, or diluent.
55. A method for alleviating a symptom of a disorder characterized by abnormal levels of cellular proliferation in a tissue comprising: administering a soluble ephrin receptor to a patient suffering said disorder, wherein the administered soluble ephrin receptor modulates proliferation of cells in the tissue, thereby alleviating the symptom of the disorder.
56. The method of claim 55 wherein the soluble ephrin receptor comprises a ligand binding domain of an ephrin receptor.
57. The method of claim 55, wherein the soluble ephrin receptor or a fragment thereof is joined to a heterologous amino acid sequence.
58. The method of claim 57, wherein the heterologous amino acid sequence comprises a constant domain of an immunoglobulin.